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Food Insecurity, Race, and Adolescent Non-Alcoholic Fatty Liver disease in NHANES 2001-06

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Food Insecurity, Race, and Adolescent Non-Alcoholic Fatty Liver disease in NHANES 2001-06

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Abstract

Introduction: Non-Alcoholic fatty liver disease (NAFLD) is the most common chronic liver condition in the U.S and is an emerging public health concern in adolescents. Risk factors for adolescent NAFLD remain largely unexamined.

Aim: To investigate if demographic and dietary-related factors are linked with NAFLD in adolescents.

Methods: Cross-sectional data from NHANES (2001-2006) ages 12-19 (n=4714) were analyzed. NAFLD was defined as >30 u/L ALT. Food Insecurity levels (child, adult, household), race/ethnicity, sex, BMI, and the Dietary Inflammatory Index (DII) were tested using multivariate binary logistic regression with elevated ALT (no, yes) as the dependent variable.

Results: Risk for elevated ALT among Non-Hispanic Blacks was 1.25 times greater compared to Non-Hispanic Whites (95% CI 1.00-1.57). Higher DII quartiles (i.e., increasingly pro-inflammatory) show a possible link with elevated ALT (e.g., Q2vsQ1: OR=1.23, 95% CI .95-1.59; Q3vsQ1: OR=1.31, 95% CI 1.01-1.69; Q4vsQ1: OR=1.14 95% CI .88-1.48). Findings regarding food security were inconclusive**.**

Conclusion: This study is the first report, to our knowledge, that Non-Hispanic Blacks might be at greater risk for adolescent NAFLD compared to Non-Hispanic Whites. Lack of an association with Hispanics is inconsistent with prior research in adults, however. Future research is suggested to understand underlying risk factors linked with disparate risk. A potential association with a pro-inflammatory diet also warrants further study. We posit that inconclusive results about food insecurity might due to lower rates of obesity, a known risk factor for NAFLD, in this vulnerable population.

Competencies Addressed

Foundational Competencies

1. Apply epidemiological methods to the breadth of settings and situations in public health practice

3. Analyze quantitative and qualitative data using biostatistics, informatics, computer-based programming and software, as appropriate

4. Interpret results of data analysis for public health research, policy, or practice

6. Discuss the means by which structural bias, social inequities and racism undermine health and create challenges to achieving health equity at organizational, community and societal levels

21. Perform effectively on interprofessional teams

22. Apply systems thinking tools to a public health issue

Concentration-specific Competencies

3. Demonstrate high personal and professional ethical conduct in contributing to team-based activities

Introduction

Overview. Non-Alcoholic Fatty Liver disease (NAFLD) is a chronic liver condition caused by excess accumulation of fat in the liver. NAFLD is the most common chronic liver disease in children and adults in industrialized countries and is associated with an increased risk of cardiovascular disease, type 2 diabetes (T2D), and liver-related morbidity (Alkhouri & Kay, 2012). NAFLD can be divided into 2 subtypes: 1) Simple fatty liver disease, which is characterized by no inflammation or cell damage; and 2) Non-alcoholic steatohepatitis (NASH) where inflammation and cell damage do occur. The difficulty with NAFLD and NASH is the lack of identifiable symptoms, so they are considered silent diseases. While the direct cause of NAFLD is not known, it has been reported that prevalence increases with the occurrence of obesity, T2D, insulin resistance, and high lipid disorders. Pediatric NAFLD is thought to affect around 1 in 10 children in the United States and 34% of children with obesity (Draijer et al., 2019). More research needed is to determine the lifestyle risk factors, improvements in screening methods, and potential treatment therapies. An unexplored potential risk factor is the association with food insecurity as a predictor for pediatric NAFLD due to its relationship with poor diet and obesity, which is what forms the research question of this thesis. Other variables that have been found to be potential factors such as race/ethnicity, c-reactive protein (CRP), the dietary inflammatory index (DII), body mass index (BMI) we examined for the cohort.

Health Outcomes. NAFLD is characterized with metabolic syndrome (MetS) along with other entities such as diabetes, being overweight, high cholesterol, and high blood pressure (Kumar, Priyadarshi, & Anand, 2020). The two subtypes, nonalcoholic fatty liver (NAFL) and NASH are differentiated by the occurrence of inflammation or cell damage. The gold standard for NAFLD

diagnosis is through histology of the liver tissues, most recently utilizing the NAFLD activity score developed by the Pathology Committee of the NASH Clinical Research Network. The score is used to determine the amount of fat accumulation, inflammation, and fibrosis (Lindenmeyer & McCullough, 2018). To accurately diagnose NAFLD, all other potential causes of liver steatosis such as alcohol consumption, hemochromatosis, viral hepatitis, and certain hereditary disorders must be excluded (Chalasani, 2012). It is important to make a histological distinction between the subtypes because therapeutic interventions for treatment vary for each, and as the disease progress, those afflicted have increased risk of fibrosis, cirrhosis and end-stage liver disease (Lindenmeyer & McCullough, 2018). The spectrum of diagnosis ranges from simple steatosis (SS), to NASH, and then ultimately hepatocellular carcinoma (HCC). This progression is still incompletely defined as SS is now shown to be more progressive than originally believed. Along with the variants associates with MetS, some genetic polymorphisms have a significant impact on the progression (Kumar et al., 2020).

There have been many studies looking into the progression of NAFL versus NASH to better understand the connection between them. A 2006 study by Ekstedt found that NASH is associated with a reduced survival more than NAFL and death being most commonly cause by cardiovascular disease. This study also found that elevated liver enzymes such as Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) is a risk factor for developing end-stage liver disease (Ekstedt, 2006). Initially it was thought that NAFL could not progress to NASH, but a 2013 study found that, especially in the presence of risk factors, patients with NAFL could progress to NASH with fibrosis. Those with any degree of mild inflammation or fibrosis were at higher risk for progression than those with only liver fat build-up. Progression occurred in tandem with elevated ALT, higher weight gain, and higher diabetes incidence (Pais

et al., 2013). The final stage of NAFLD, HCC, is the most common type of primary liver cancer and is the fastest-rising cause of cancer-related deaths in the US. HCC occurs most often in those with chronic hepatitis C (HCV), hepatitis B (HBV), NAFLD, diabetes, or heavy alcohol drinkers. The incidence of HCC has been increasing in North America but decreasing in Japan and parts of China, which were traditionally high-risk regions (Kulik & El-Serag, 2019). A 2015 study by Kallwitz et al., found that this trend is likely due to higher rates of HCV, HBV, and NAFLD and that Hispanic Americans with HCV or NAFLD have a higher risk of progression to cirrhosis and HCC (Kallwitz et al., 2015).

NAFLD has long been considered a display of MetS in the liver. Diagnosis of MetS requires confirmation of 3 of the 5 following factors: obesity, hypertension, low HDL cholesterol, hypertriglyceridemia, and fasting hyperglycemia. Determination is made based on waist circumference over 102 cm for males and 88 for females, blood pressure over 135/85, fasting blood glucose over 100 mg/dl, HDL under 40 mg/dl in males and under 50 mg/dl in females, and triglycerides over 150 mg/dl (Sumner & Cowie, 2008). NADLF has been found to present clinical and laboratory data like that of diabetes and obesity, including insulin resistance, increased triglycerides, increased uric acid, and low HDL cholesterol (Marchesini et al., 2001). In 2003, Marchesini et al. documented that MetS was a high risk for NASH and that increasing prevalence of obesity and diabetes in the population would lead to a large risk of liver failure in the coming decades which is what has occurred (Marchesini et al. 2003). Many studies have strongly associated ALT with NAFLD and NAFLD is the common cause of unexplained mild ALT elevation (Liu, Que, Xu, & Peng, 2014). Liu et al. suggest that when elevated ALT is present without viral hepatitis or excessive alcohol consumption, NAFLD is the cause.

Currently, NAFLD is known to be a risk factor with many diseases such as type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), chronic kidney disease (CKD), polycystic ovarian syndrome, obstructive sleep apnea, psoriasis, osteoporosis, stroke, acute pancreatitis, and recently with sarcopenia (Kumar et al., 2020). NAFLD has also become the second most common indication for liver transplantation (LT) after chronic hepatitis C, with new LT waitlist registrants increasing by 170% from 2004-2013 (Lindenmeyer & McCullough, 2018). NAFLD is both a cause in the development of T2DM, but also a consequence of pre-existing T2DM. Two large meta-analyses confirmed this relationship, with 58% of NAFLD patients developing T2DM (Kumar et al., 2020; Musso, Gambino, Cassader, & Pagano, 2011). The risk of T2DM was found to be three times higher for patients with NASH versus SS and showed increased risk of NAFLD progression to NASH and HCC. Overall, the coexistence of diabetes and NAFLD in a patient increases risk of progression and complications related to both diseases. Increased risk of CVD has consistently been seen with studies showing increased carotid artery thickness, increased arterial stiffness, impaired flow of dilated blood vessels, and endothelial dysfunction ((Kumar et al., 2020). A 2016 study found that progression of NAFLD is associated with increased risk of subclinical carotid atherosclerosis (Sinn et al., 2016). Studies confirm the association of increase CVD prevalence, but more research is needed to determine the association of increased CVD mortality and if these associations are due to shared risk factors or NAFLD itself is and additional risk for CVD (Kumar et al., 2020). A 2014 meta-analysis on 64,000 subjects found NAFLD was associated with a 2-fold increase in incident and prevalent CKD, with more progressive forms such as NAFL with fibrosis and NASH being more positively correlated with CKD in comparison to SS (Musso et al., 2014). The associations recognized in the review by Kumar et al. along with those by Lindenmeyer & McCullough

document the increasing risk and associations of NAFLD, with projections showing an ever-increasing global impact.

Treatment of NAFLD includes working to treat the liver disease along with lifestyle modifications to help with the associated risk factors of diabetes, obesity, and hyperlipidemia. Chalasani et al. found that weight loss can reduce fat in the liver, inflammation and scarring and most clinicians are recommended to get patients to lose weight through healthy food choices and increase physical activity (Chalasani, 2012). Losing 3-5% of body weight can reduce fat in the liver and it was found that a low-calorie diet along with increased physical activity can improve NAFLD and NASH outcomes (Ahmed, Wong, & Harrison, 2015). It has also been seen that exercise alone, without weight loss, can improve NAFLD outcomes, with a combination of exercise, medication, and diet changes being the most effective (Oliviera, de Lima Sanches, de Abreu-Silva, & Marcadenti, 2016). Weight reduction through bariatric surgery has shown benefits for NAFLD patients as well. A medication considered for treatment is metformin which is commonly prescribed for diabetic patients but studies on the effectiveness of metformin for NAFLD have shown mixed results (Sao & Aronow, 2018). Generally, there is no standard pharmacological treatment, with the standard options being to target weight loss through diet changes and physical activity. This is most applicable for those with NASH as it has been found that a loss of >7% body fast is associated with disease regression. The main difficulty in treatment is implementing the lifestyle changes in clinical care and the daily life of the patient (Romero-Gomez, Zelber-Sagi & Trenell, 2017). With more big data analyses being conducted on this topic, the true global disease burden can be seen with the increase in progression, associated conditions, and need for enhanced treatment and prevention options.

Epidemiology. The spread of NAFLD can be seen worldwide but the exact incidence and prevalence are unknown due to the lack of accuracy in the noninvasive markers related to the condition. Liver biopsy for histology is invasive and expensive so noninvasive measures such as liver-associated tests, imaging, or spectroscopy methods have been considered (Ong, & Zobair, 2007). Community surveys have utilized ultrasonography or proton NMR spectroscopy whereas studies based on elevated liver enzymes were found to systematically underestimated the true prevalence. Overall, global prevalence of NAFLD is currently estimated to be 24% as of 2018 (Younossi et al., 2018). Through data from the National Health and Nutrition Examination Surveys (NHANES) from 1988 to 2008, it has been seen that NAFLD prevalence has doubled in the US from 46.8% to 75.1% of chronic liver disease cases. It is projected that this will increase by 21% by 2030, leading to an overall prevalence of 33.5% in the general population (Kumar et al., 2020).

Globally, the highest rates are from South America (31%), the Middle East (32%), Asia (27%), the USA (24%), and Europe (23%). The least common incidence is reported in Africa with 14%. A 2016 meta-analysis conducted by Younossi et al. determined NAFLD prevalence in the USA through ultrasonography, Fatty Liver Index (FLI), and the International Classification of Diseases (ICD). The findings followed that disease diagnosis solely based on ICD or blood testing led to underreporting. This study found that prevalence varied by ethnicity, with Hispanic American having the highest rates, followed by Americans of European descent and African Americans. While unconfirmed, this disparity is thought to be due to socioeconomic disparities, along with the possibility of genetic factors and presence of MetS. This finding is supported through many previous studies but contradicts the findings of higher obesity and hypertension in African American patients and Serif et al., found that there is a concern that the disease burden

of NAFLD on the African American population is actually underestimated (Sherif et al., 2016). Another assessment of NHANES data found that NAFLD posed a significantly higher risk in black adolescents but for adults, education was inversely related (Jaradat, 2017). A 2017 study found NAFLD prevalence in the US as 30% with 10.3% of these cases having advanced fibrosis. This study defined NAFLD as subjects having a US Fatty Liver Index (USFLI) greater than 30 which has been shown to correlate with NAFLD diagnosed through ultrasound. It was found that subject with NAFLD were more likely to have higher ALT and AST (Le et al., 2017).

NAFLD without the presence of obesity is termed "lean NAFLD". This was initially described in Asian populations and believed to be more benign than NAFLD, but studies have found that patients with lean NAFLD have impaired insulin sensitivity, increased cardiovascular risk, and increased liver fat levels. A study by Fracanzani et al. in 2011 found that 55% of patients without obesity did have NASH and fibrosis and a study by Leung et al. in 2017 found that 51.9% of obese versus 43.5% of non-obese patients had NASH suggesting that obesity might not be as associated with fibrosis progression. Since it is harder to diagnose and identify risk factors for those with lean NAFLD, further research is needed into the topic (Younossi et al., 2018).

Pediatric NAFLD. Pediatric NAFLD is defined as chronic hepatic steatosis in children when no occurring with genetic/metabolic disorders, infections, alcohol consumption or malnutrition. In most children, NAFLD is associated with insulin resistance, obesity, high triglycerides, and low HDL cholesterol levels (Vos et al., 2017). As obesity in children increased worldwide, so has the prevalence rates of pediatric NAFLD. In the general pediatric population NAFLD presents at 7.6% while in the obese pediatric population it is 34.2% (Anderson et al., 2015). It has been seen

that 66% of children with biopsy proven NAFLD had one or more metabolic risk factors, with T2DM and insulin resistance having the strongest link (Draijer et al., 2019). Children with NAFLD are at high risk of progressing to end-stage liver disease and cases of liver transplantation (Alkhouri et al., 2016) While this public health problem is severely increasing, there is a large lack of research in the area of pediatric NAFLD and many unknowns.

From a special report by Hatton et al. (2018): "Pediatric NAFLD has previously been ascribed to three broad histological types: (1) Centrilobular steatosis, ballooning degeneration and inflammation with perisinusoidal fibrosis; (2) periportal inflammation and steatosis with portal fibrosis; and (3) overlap between 1 and 2." (p. 961). Type 2 is more common in children than adult NASH but there is little known on why or how NASH is different between the populations. It is unknown how to stratify children into risk groups for interventions based on related diseases such as CVD and diabetes and it is thought that pediatric NASH has a different immune process than adult NASH, but it is not well understood. The direct cause of pediatric versus adult NAFLD is different and further research is needed to determine appropriate diagnosis methods and treatment. It has been found that prenatal and postnatal factors contribute to the development of pediatric NAFLD, but the etiology and pathophysiology are not well defined (Hatton et al., 2018). A 2013 study found support for the racial/ethnic differences in the link between MetS and NAFLD in adolescent populations. It found that the prevalence of MetS in was 10.6% in Hispanics, 8.4% in Whites and 4.2% in Blacks and this was paralleled with 13.7% in Hispanics, 8.6% in Whites and 5.2% in blacks for elevated ALT. ALT was defined as the best marker for NAFLD as an alternative to biopsy as ALT had a .92 sensitivity to identifying fatty-fibrotic findings on ultrasound. This study also found that adolescents with MetS with 7.8 times more likely to have elevated ALT (DeBoer et al., 2013). The use of ALT as

a marker for pediatric NAFLD has been supported by the North American Society for Pediatric Gastroenterology, Hepatology & Nutrition in a clinical practice guideline released in 2017. The ALT assay has been standardized across facilities but the cut-off points for normal ALT levels has not. In the US, the cut-off has been defined as 22 mg/dl for girls and 26 mg/dl for boys while in Canada, the upper limit for normal ALT was 30 mg/dl for children 1-12 years old and 24 mg/dl for children 13-19 years old. NASH was found to be associated with ALT greater than 8-U/L (Vos et al., 2017).

Children with NAFLD and fibrosis are at higher risk of long-term liver complications due to their life span and as diagnosis is difficult without biopsy and treatment is limited to lifestyle interventions, the pediatric NAFLD population is at very high risk for complications. The ideal solution is obesity prevention early on, further research into this specific population, and increased awareness about this growing public health issue (Draijer et al, 2019). The pediatric obesity rate has risen from 5% to 16.9% from 1960 to 2010 and since weight gain during childhood carries a higher risk of NAFLD than weight gain in adulthood, risk of progressive NAFLD such as fibrosis, cirrhosis, HCC, end-stage liver disease, and liver-related death are increased (Younossi et al., 2018).

Even though pediatric NAFLD has such high prevalence and poor outcomes, it remains under-studied and under-recognized, allowing this trend to continue to increase for the foreseeable future. There are unmet needs in the areas of screening, diagnosis, treatment, and awareness. For those whom on the extreme end of the obesity spectrum, there are no non-surgical options and there is a lack of collaboration between clinical specialties and targeted therapeutic interventions that could improve patient outcomes (Temple et al., 2016). More research is needed to find novel biomarkers and therapeutic agents to avoid the current risk of

long-term morbidity. The pediatric population is more vulnerable to genetic and environment factors so further research is also needed into the perinatal and postnatal stressors that increase risk of NAFLD onset (Goldner & Lavine, 2020). Dietary factors have been found to be associated with pediatric NAFLD and a study conducted in Korea found that children with suspected NAFLD were found to have elevated urinary sodium levels and elevated cholesterol intake (Kim & Lee, 2020). This is an area for further research to be able to best determine preventive dietary measures. In Dutch hospitals a survey was conducted to determine pediatric NAFLD screening practices and found that while widely performed, there is no uniform protocol to follow (Draijer et al., 2020). Overall, despite the high prevalence and serious complications, pediatric NAFLD is not as widely researched as adult onset NAFLD and leaves room for further exploration.

Food Insecurity. As defined by the US Department of Agriculture (USDA), food security (FS) is defined as a household always having access to enough food for all members of the household to lead an active, healthy lifestyle. Food insecurity is defined as households that were uncertain of having or being unable to get enough food at times due to lack of money or other resources. Low food security is defined as households getting enough food to avoid substantially disrupting eating patterns or food intake by use of coping strategies such as a less varied diet, a food assistance program, or emergency food from a food pantry. Very low food security is defined as households that had a disruption of normal eating patterns for one or more member of the house along with reduced food intake due to lack of money or other resources. In 2018, 11.1% of households were food insecure, 6.8% were low food security and 4.3% were very low food security at some time during the year. These values are all lower than the food insecurity figures

for 2017 (Coleman-Jensen et al., 2019). Food insecurity affects 35% of low-income US households and has been associated with increased risk of diabetes, hypertension, obesity, and CVD (Golovaty et al., 2020). While these conditions have been shown to be strongly linked to NAFLD, there has been only one study looking into the correlation of food insecurity and NAFLD risk. The 2020 study by Golovaty et al. examined food insecurity as an independent risk factor for NAFLD in low-income adults. It was found that 29% of adults were food insecure and that food insecure adults were more likely to have NAFLD and advanced fibrosis than adults who were food secure (Golovaty et al., 2020). This is a huge area of potential research to further our understanding of the risk factors associated with NAFLD and improve upon recommendations for intervention and treatment.

Systems Thinking. NAFLD is the most common form of chronic liver disease and is likely to become the leading cause of liver failure and liver transplantations in the pediatric populations. This disease is widespread and highly interconnected with other MetS disorders such as obesity, diabetes, and CVD. The main issue in the area of pediatric NAFLD is the lack of research. Currently, the main treatment option is weight loss through diet and exercise. If more research is conducted into the etiology and pathophysiology, the is potential for alternative diagnostic tests, more interventions, better treatment options, and more awareness about the associated conditions. The increase in pediatric cases is tied to the increase in obesity worldwide. The obesity epidemic is due to the current food habits and food available to people around the world. If people are more food secure (having access to fresh, health, inexpensive options regularly), then there is no need to purchase fast food or other unhealthy options. This is impacted by the socioeconomic levels of families, the local environment they live in and access to care, and

knowledge on how to be and stay healthy. For children, funding and implementation of the national school breakfast, lunch, summer programs could heavily impact food security. Government policy based on the findings of the scientific community regarding food security, food deserts, obesity, NAFLD, and risk factors could drastically change the obesity epidemic. If policy could be enacted for better regulations on fast food companies and increasing the number of supermarkets with fresh food in areas that need it. For people who need assistance, policy impacts the availability of Supplemental Nutrition Assistance Program (SNAP), formerly known as food stamps, and stipends. Policy can also impact the funding that goes into research and the funding that goes into other stakeholders such as hospitals, physicians, local health departments, and insurance companies. NAFLD has many comorbidities which impact these stakeholders when treatment is needed for NAFLD, CVD, and diabetes. With the increase in association for liver transplantation, hospitals, physicians, insurance companies, and the overall cost on the healthcare system increases. If the initial risk factors can be intervened upon, then all the following procedures and costs could be avoided.

The public health issue of rising pediatric NAFLD is not a simple problem to treat with a one-step solution, but a complex issue that ties into many stakeholders in the healthcare system. By increasing awareness on the large impact of the disease, it is more likely that particular research will be conducted in the unmet areas, better policy can be enforced to improve structural and environmental issues, and a more holistic approach can be taken to try and reduce the global burden of this disease.

Prevention, Diagnosis, and Treatment of Emerging Incidence of NAFLD in Adolescents

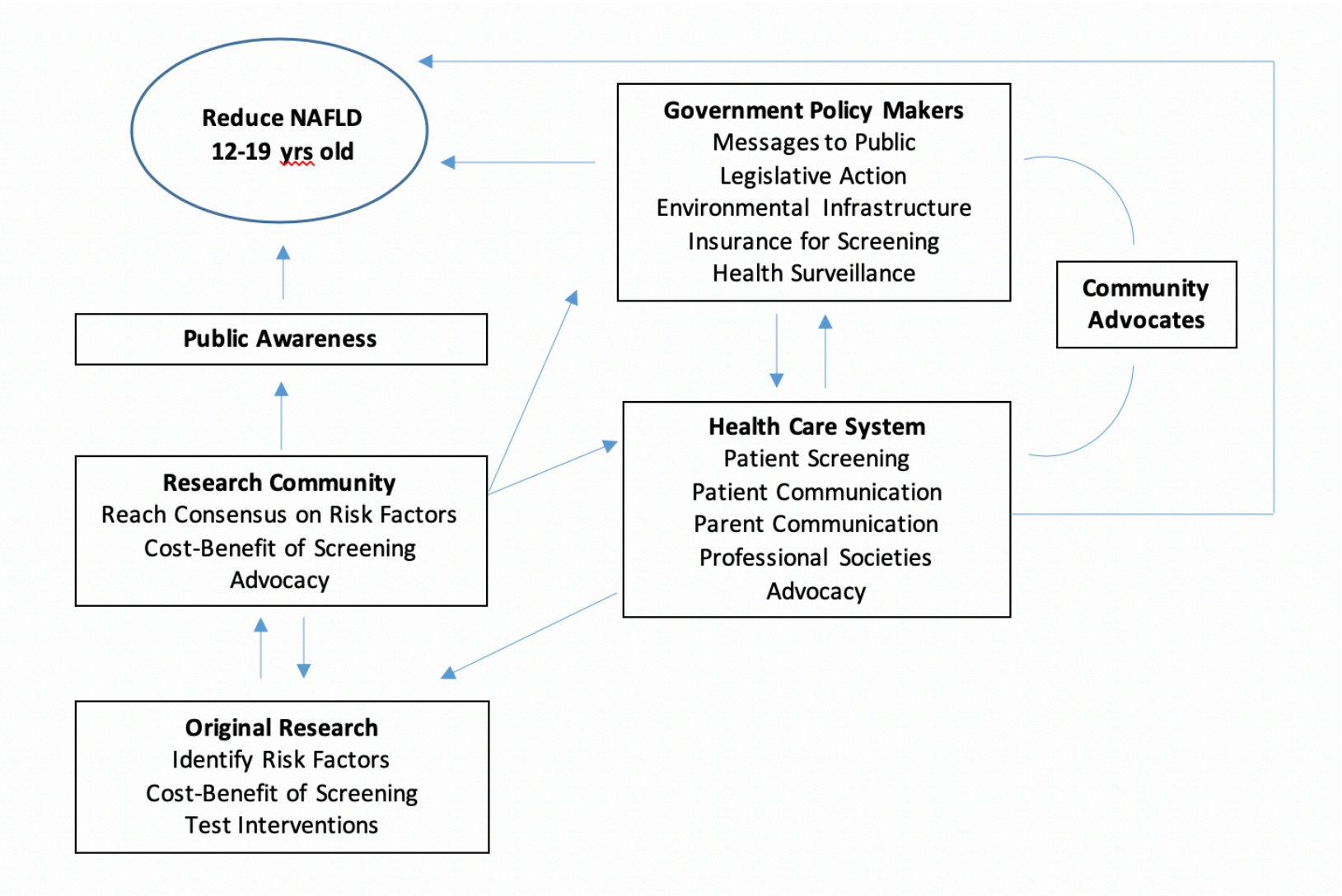

Figure 1. Systems Thinking Map

Statement of the Problem. There is very little understanding of why certain people get NAFLD and why in some people this condition is exacerbated to levels of extreme cirrhosis. There is also very little known about the symptoms of NAFLD, making it very difficult to identify at-risk populations. NAFLD has become increasingly prevalent in the pediatric population. Previous thesis work identified that NAFLD is more prominent in black adolescents and in adults with less than a college degree (Jaradat, 2017). This thesis also found that the three-fold greater prevalence of elevated uric acid in both age groups, which warrants further research and might have translational value for screening for liver disease. By adding the risk factor of food insecurity into this study, there is a likelihood to more deeply understand a possible underlying factor associated with a racial difference.

Rates of pediatric NAFLD are currently following the rising rates in childhood obesity, which is a well-established public health problem. Many studies have found that food insecurity is tied to obesity. If food insecurity is identified as a social determinant of NAFLD, the findings could add to the growing evidence about the harms of food insecurity and shape future public policies to increase awareness and promote improvements, especially in highly impacted populations. If correlations are found, then there is a high possibility that structural bias, social inequities, and racism could be tied to the food insecurity predictors and systems thinking will need to be applied to the findings to understand the interactions of these aspects, and how we can use these findings to potentially reduce prevalence of pediatric NAFLD. As a disease of serious long-term consequences, new causative information about NAFLD is important, especially given the lack of studies present on pediatric NAFLD.

Methods

Sample. All data analysis was conducted using the continuous 2001-2006 NHANES data set. NHANES is a population-based surveillance program conducted by the National Center for Health Statistics (NCHC) that has been continuously conducted since 1999. (***Please note:*** Dr. Swede has received blanket approval from the UCH IRB for use of NHANES datasets under Exempt Status, i.e., non-human subjects research, for use in student and faculty research projects.) The survey includes a questionnaire, an interview, an at-home medical examination, and a mobile center for laboratory tests. The data includes a variety of variables related to physical and environmental conditions that tie to prevalent health conditions in the U.S. For this analysis, participants were included if they were 12-19 years old (n=7078) and had the NAFLD indicator marker (ALT) documented. Pregnant females were excluded per previously conducted studies examining ALT and NAFLD (Umehara, 2018). The study sample (n=4714) consists of males (n=2412) and non-pregnant females (n=2302) with valid ALT results, n=3921 for normal ALT and n=793 for elevated ALT.

Variables. In the existing dataset, NAFLD was defined by two established blood markers, ALT and AST. Per the NASPGHAN clinical practice guidelines, ALT is the recommended standard marker for NAFLD (Vos et al., 2017). In this study, normal ALT was defined as lower to equal to 30 U/L and elevated ALT was defined as greater than 30 U/L. As the NASPGHAN guidelines had discrepancies for US versus Canadian recommendations, we followed thresholds as described in DeBoer et al. (2013). Several independent variables were examined in this study to ensure no selection bias along with no sample bias as evident in Table 2. Demographic characteristics examined were sex and race/ethnicity. Education could not be examined due to lack of data in the selected study cohort.

C-reactive protein (CRP) is an inflammatory marker and has been linked to CVD and obesity (Barinas-Mitchell et al., 2001). The original CRP data was sorted as low risk if <1 mg/L, average risk between 1 and 3 and high risk above 3 mg/L. CRP value >10 mg/L were excluded as it is indicative of an acute infection. This data was transformed into quartiles of <.09 (Q1), .09-.23 (Q2), .23-.53 (Q3) and >.52 (Q4) to allow for better population distribution analysis. BMI was categorized as underweight (<18.5), normal (18.5-24.9), overweight (25.0-29.9), obese (30.0-34.9) and morbidly obese (>35) per CDC guidelines.

Dietary inflammatory Index (DII) is based on 8 pro-inflammatory and 8 anti-inflammatory components to assess the inflammatory potential of dietary factors (Kanauchi et al., 2019). DII was developed to provide a quantitative means for assessing the role of diet in relation to health outcomes designed to be applicable across all human studies with adequate dietary assessment. DII is a continuous variable which was transformed into quartiles for population comparison analysis with the 1st to 4th quartile going from less to more proinflammatory (Hébert et al., 2019).

NHANES has created summary variables that characterize food insecurity using U.S. Household Food Security Survey Module split into household, adult, and child:

Household: whether the statement was often true, sometimes true, or never true for (you/your household) in the last 12 months

1) "(I/We) worried whether (my/our) food would run out before (I/we) got money to buy more." Was that often true, sometimes true, or never true for (you/your household) in the last 12 months?
2) "The food that (I/we) bought just didn't last, and (I/we) didn't have money to get more." Was that often, sometimes, or never true for (you/your household) in the last 12 months?
3) "(I/we) couldn't afford to eat balanced meals." Was that often, sometimes, or never true for (you/your household) in the last 12 months?

Adult:

1) In the last 12 months, since last (name of current month), did (you/you or other adults in your household) ever cut the size of your meals or skip meals because there wasn't enough money for food?

2) [IF YES ABOVE, ASK] How often did this happen—almost every month, some months but not every month, or in only 1 or 2 months?
3) In the last 12 months, did you ever eat less than you felt you should because there wasn't enough money for food?
4) In the last 12 months, were you every hungry but didn't eat because there wasn't enough money for food?
5) In the last 12 months, did you lose weight because there wasn't enough money for food?
6) In the last 12 months, did (you/you or other adults in your household) ever not eat for a whole day because there wasn't enough money for food?
7) [IF YES ABOVE, ASK] How often did this happen—almost every month, some months but not every month, or in only 1 or 2 months?

Child:

1) "(I/we) relied on only a few kinds of low-cost food to feed (my/our) child/the children) because (I was/we were) running out of money to buy food." Was that often, sometimes, or never true for (you/your household) in the last 12 months?
2) "(I/We) couldn't feed (my/our) child/the children) a balanced meal, because (I/we) couldn't afford that." Was that often, sometimes, or never true for (you/your household) in the last 12 months?
3) "(My/Our child was/The children were) not eating enough because (I/we) just couldn't afford enough food." Was that often, sometimes, or never true for (you/your household) in the last 12 months?
4) In the last 12 months, since (current month) of last year, did you ever cut the size of (your child's/any of the children's) meals because there wasn't enough money for food?
5) In the last 12 months, did (CHILD'S NAME/any of the children) ever skip meals because there wasn't enough money for food?
6) [IF YES ABOVE ASK] How often did this happen—almost every month, some months but not every month, or in only 1 or 2 months?
7) In the last 12 months, (was your child/were the children) ever hungry but you just couldn't afford more food?
8) In the last 12 months, did (your child/any of the children) ever not eat for a whole day because there wasn't enough money for food?

Both adult and household food security were defined per USDA regulations as fully food secure, marginal food security, low food security, or very low food security. The household measure uses all 18 items, or 10 items for households without children, consistent with the CPS categorical measure. The four categories created for household food security are: food secure, marginally food secure, food insecure without hunger, and food insecure with hunger. The adult measure uses 10 items and categories are the same as those used for the household measure. For adult-only households, the household and adult measures are identical (NHANES 2001-2002,

2004). For this analysis, the categories correspond to full food security, marginal, low and very low food security respectively in the attached tables.

The child measure categorization is based upon “Measuring Children’s Food Security in U.S. Households, 1995-99” (ERS research report) which uses the 8 child-referenced items to classify households into two categories, no or insufficient evidence of hunger versus clear evidence of hunger. In order to keep consistent with the household and adult measures, NHANES data are grouped into four categories. The first category in the ERS report is separated into three categories 1) food quantity and quality unaffected, 2) marginally food secure, and 3) food insecure without hunger. The most severe category is scored the same as that in the ERS report labeled “child food insecure with hunger” (NHANES 2001-2002, 2004). For the 2003-2006 surveys, this was updated to the categories 1) food quality & quantity unaffected, 2) reduced food quality or quantity, 3) reduced food quality and quantity, and 4) severely reduced food quality and quantity (National Health and Nutrition Examination Survey 2003-2004, 2007).

Statistical analysis was conducted with Statistical Package for the Social Sciences (SPSS) version 26. Descriptive analyses, t-Tests for continuous dependent values and Chi-Square tests for categorical variables, were conducted to examine the prevalence of study variables by NAFLD status. Univariate and multivariate logistic regression was conducted to find which variables predict NAFLD (yes, no) in the pediatric population with a 95% confidence interval. In keeping with the recent policy from the American Statistical Association, we will report specific p-values for each test, and not use a threshold cut-point.

Results

Table 1 describes the demographic and clinicopathological characteristics of our study population. The study sample (n=4714) consists of males (n=2412) and non-pregnant females (n=2302) with valid ALT results, n=3921 for normal ALT and n=793 for elevated ALT. The overall prevalence of NAFLD as defined by elevated ALT >30 U/L was 793/3921 or 20.22%. Prevalence was similar across sexes with 17.2% of males and 16.5% of females showing elevated ALT (p=.521). Prevalence was varied across race/ethnicity with Non-Hispanic Whites (NHW) having a much lower prevalence, 15.0%, than Non-Hispanic Blacks (NHB),18.8%, the Hispanic population at 16.3% and other races/ethnicities at 17.3% (p=.055). Within the CRP quartiles high ALT ranges from 16.5% (Q2) to 17.4% (Q4) with no clear pattern (p=.785). Similarly, with BMI, 16.5% of the underweight, 17.0% of normal weight, 16.4% overweight, 18.3% of obese, and 14.9% of morbidly obese population showed elevated ALT levels (p=.831). DII results across quartiles were 15.4% (Q1), 17.1% (Q2), 17.5% (Q3), and 16.9% (Q4) for elevated ALT (p=.576). For child food security, elevated ALT levels were found at 17.1%, 14.7%, 17.4%, and 20.6% for Unaffected, Reduced Quality or Quantity, Reduced Quality and Quantity, and Severely Reduced Quality and Quantity of FS, respectively (p=.549). Adult and household FS showed similar elevated ALT values per level of food security. Adult FS had elevated ALT in 16.5% of the fully food secure, 18.2% in marginally food secure, 16.3% in low food security, and 18.7% in the very low food security populations (p=.568). Household food security was the final characteristic analyzed, with 16.4%, 19.1%, 16.6% and 18.1% of the full, marginal, low, and very low FS populations respectively displaying elevated ALT.

Table 2 describes the same demographic and clinicopathological characteristics of our study population as Table 1 but is comparing the populations of those included in the sample (n=4714) versus those who were excluded (n=2364) such as pregnant females or those with no ALT values. This was done to ensure there was no selection or sample bias in defining the sample cohort. Of the total 7078, 4714 samples (66.6%) were included and 2364 (33.3%) were excluded. Across all the variables that were examined, the included samples were fairly representative in comparison to the excluded samples, for example, included males were 51.2% of the cohort compare to 47.8% excluded. The largest discrepancies were in CRP and BMI. For CRP, the breakdown between the quartiles was 60.7%, 14.1%, 8.8% and 7.7% included versus 51.1%, 12.9%, 9.8%, and 8.8% excluded for Q1 to Q4 respectively. In the BMI categories, the included sample breakdown was 14.3%, 54.4%, 18.2%, 7.6%, and 5.5% for the underweight to morbidly obese population respectively. This is compared to the excluded breakdown of 12.6%, 52.2%, 17.5%, 10.5%, and 7.2%. For a majority of the samples the included participants were representative respective to the excluded cohort, the largest variation being a 9.6% difference in the Q1 selection sample for CRP.

Table 3 stratifies the study population by race/ethnicity. For sex, Non-Hispanic Black rates of elevated ALT were 18.7% for males and 18.9% for females (p=.893). In CRP, Non-Hispanic Black elevated ALT was 19.8%, 14.9%, 16%, and 20% in quartiles 1 to 4, respectively. Non-Hispanic Black elevated ALT rates for BMI were found to be 18.7% for underweight, 18.9% for normal weight, 20.7% for overweight, 18.9% for obese, and 13.1% for morbidly obese populations. Across DII quartiles, Non-Hispanic Black elevated ALT was 18.3%, 20.6%, 16.7%, and 19.5%. For child food security, prevalence of elevated ALT in the severely reduced quality and quantity was the highest of all categories within Non-Hispanic Blacks at 22%. Adult food

security elevated ALT levels for Non-Hispanic Blacks were 18.6%, 20.3%, 17.8% and 21.6% for full, marginal, low, and very low food security populations. Household food security elevated ALT levels for Non-Hispanic Blacks were 18.4%, 20.8%, 19.6% and 20.5% for full, marginal, low, and very low food security populations.

Table 4 presents results of univariate and multivariate models of a binary logistic regression on all the variables previously examined. Non-Hispanic Black participants were 1.31 times more likely (95% CI 1.07-1.59) to have elevated ALT compared to Non-Hispanic Whites in the univariate model and 1.25 times more likely (95% CI 1.00-1.57) in the multivariate model. Increased DII score as stratified by quartile (i.e., increasingly pro-inflammatory) were linked to elevated risk of elevated ALT (e.g., Q2vs Q1: OR=1.23, 95% CI .95-1.59; and, Q3 vs Q1, OR=1.31, 95% CI 1.01-1.69.) Adolescents characterized as having reduced quality or quantity of food appeared less likely to have elevated ALT compared to children rated as unaffected by insecurity (OR=0.63, 95% CI 0.37-1.09). Similarly, those characterized on the adult scale as being marginally insecure were at a possible reduced risk compared to those fully secure (OR=0.58, 95% CI 0.22-1.51). In contrast, using the household level assessment, adolescents marginally food insecure were at possible increased risk for elevated ALT compared to the fully secure (OR=2.08, 95% CI 0.80-5.41).

Discussion

Prevalence of NAFLD. The prevalence of elevated ALT in the overall cohort was 20.22%. This did not vary noticeably for any variable except for race ethnicity. Non-Hispanic Blacks had the highest elevated ALT of 18.8% in comparison to Non-Hispanic Blacks at 15.0%, Hispanics at 16.3% and other at 17.3% (p=.055). Elevated ALT was indicated as levels higher than 30 U/L but in the future, this study could be modified to the updated cut-offs of 22 mg/dl for girls and 26 mg/dl based on the clinical practice guideline released in 2017 as this could have an impact on the prevalence proportions for boys. As different studies use a variety of cut-off levels, 22 and 26 could be reference lab values for evaluating elevated liver enzymes due to medical conditions like viral hepatitis, autoimmune hepatitis, obstructive liver disease and others. However, these levels are for clinical evaluation, in this study we are using epidemiological evaluation. Some epidemiological studies used 40 and got similar results (Vos et al., 2017).

Food Insecurity and NAFLD. Estimated risks associated with Food Security were inconclusive and are therefore suggestive of inconsistency across the three measures. Among the child and adult assessments of food security, adolescents in the “reduced quality or quantity” or “marginal” food security respectively appeared less likely to have elevated ALT compared to those rated as fully food secure. In contrast, using the household level assessment, adolescents categorized as marginally food insecure were at possible increased risk for elevated ALT compared to the fully secure. While all food security analyses were not convincing due to lack of statistical significance, unravelling contrasting trends might be explained by more sophisticated analyses examining links among variables, such as factor analysis or structural equation modeling. Alternatively, it is possible that the impact of insecurity on NAFLD risk is a longer-term risk factor that might be revealed in prospective studies. This possibility in adolescents is consistent

with prior studies in adults linking food insecurity to the MetS and obesity, both of which have been linked to NAFLD. For example, Golovaty et al. reported a relationship between low-income adults and NAFLD. Golovaty et al. found that the dose-response relation between severity of food security and NAFLD in adults was comparable to trends with obesity and diabetes. Further research in the pediatric cohort could be done to investigate a similar dose-response relationship. An alternate explanation offered by Golovaty et al. was that worsened health status (NAFLD) causes food insecurity which is another area for future research. Regardless of the direction of the relationship between food security and NAFLD, further investigation is needed as these findings could impact potential NAFLD interventions and policy for low-income and food-insecure households.

Race/Ethnicity and NAFLD. Non-Hispanic Black adolescents had a 25% increased likelihood of elevated ALT risk compared to Non-Hispanic whites. This effect is supported by the observation that Non-Hispanic Blacks had the highest prevalence of overweight/obesity (20.7%). We observed no increased risk in Hispanics compared to White adolescents which is inconsistent with prior research in race among adults. Our null finding for the pediatric population is novel, and further clarifying research is suggested to determine if risks for children and adults differ.

Metabolic Factors and NAFLD. While CRP and BMI, have been known as metabolic indicators of diabetes and obesity, there were no significant findings when compared to elevated ALT for prevalence. Increased DII score, however, was linked to elevated risk of elevated ALT, which might find indirect support in a 2019 study found that change in diet improved intestinal permeability in patients with NAFLD and patients with lower diet adherence had higher values of DII (Biolato et al., 2019).

Strengths and Limitations. This study was conducted on a large validated sample which is nationally representative but there were several limitations. Per the data presented in Table 2, the sample selection was representative when compared to those excluded so there is minimal bias. As this was a cross-sectional study, we cannot point to data significance as causation, only correlation. Since food insecurity is a novel variable in association with NAFLD, this leaves room for further, more discrete investigation. Further limitations were lack of data for every variable investigated due to the age range limitations. This is justified as there is a large need for specific inquiry into pediatric NAFLD versus adult NAFLD. Also, the cut-offs for ALT were much higher than the current recommended ranges as a previous studies cut-off was utilized to be better able to compare the findings. Since the data sampled was 2001-2006, this could be recreated with more recent data with the most up-to-date ALT cut-offs.

Conclusion

In a cross-sectional study of US adolescents (12-19), we found that NAFLD prevalence was increased somewhat in Non-Hispanic Blacks (18.8%) in comparison to Non-Hispanic Whites (15.0%), which was supported by an observation of a 25% increased risk for elevated ALT in multivariate logistic regression. A pro-inflammatory diet appears to be a risk factor for elevated ALT in adolescents. With the inconsistency in linking NAFLD with food insecurity, we posit that this early risk factor might contribute to adult onset of this disease. Future studies are suggested to identify underlying factors linked to race that would pre-dispose adolescent onset of NAFLD. Further, we suggest that retrospective cohort analyses of early-life food insecurity might reveal a connection to adult onset NAFLD. In general, more work is required to understanding the causes of adolescent onset NAFLD so that public health interventions and policies can be developed to stem this emerging epidemic.

Table 1 Demographics and Clinicopathological Factors of participants age 12-19 by ALT status in NHANES 2001-06 (n=4714)

	Normal n=3921	High n=793	p-value
Sex			
Male (n= 2412)	1998 (82.8%)	414 (17.2%)	.521
Female (n=2302)	1923 (83.5%)	379 (16.5%)	
Race/Ethnicity			
Non-Hispanic White (n=1329)	1129 (85.0%)	200 (15.0%)	.055
Non-Hispanic Black (n=1571)	1276 (81.2%)	295 (18.8%)	
Hispanic (n=1629)	1363 (83.7%)	266 (16.3%)	
Other (n=185)	153 (82.7%)	32 (17.3%)	
CRP[1] (n=4304)			
Q1 [<.09]	2370 (82.9%)	490 (17.1%)	.785
Q2 [.09-.23]	556 (83.5%)	110 (16.5%)	
Q3 [.23-.52]	346 (83.2%)	70 (16.8%)	
Q4 [>.52]	299 (82.6%)	63 (17.4%)	
BMI[2] (n=4620)			
Underweight [<18.5]	552 (83.5%)	109 (16.5%)	.831
Normal [18.5-24.9]	2086 (83.0%)	428 (17.0%)	
Overweight [25.0-29.9]	703 (83.6%)	138 (16.4%)	
Obese [30.0-34.9]	285 (81.7%)	64 (18.3%)	
Morbidly Obese [>35.0]	217 (85.1%)	38 (14.9%)	
DII[3] (n=4504)			
Q1 [< -.82]	854 (84.6%)	155 (15.4%)	.576
Q2 [-.82-.32]	958 (82.9%)	197 (17.1%)	
Q3 [.32-1.25]	937 (82.5%)	199 (17.5%)	
Q4 [>1.25]	1000 (83.1%)	204 (16.9%)	
Food Security[4] – Child (n=4022)			
Unaffected	2484 (82.9%)	511 (17.1%)	.549
Reduced Quality or Quantity	255 (85.3%)	44 (14.7%)	
Reduced Quality and Quantity	517 (82.6%)	109 (17.4%)	
Severely Reduced Quality and Quantity	81 (79.4%)	21 (20.6%)	
Food Security[4] – Adult (n=4495)			
Full	2479 (83.5%)	490 (16.5%)	.568
Marginal	481 (81.8%)	107 (18.2%)	
Low	462 (83.7%)	90 (16.3%)	
Very Low	314 (81.3%)	72 (18.7%)	
Food Security[4] – Household (n=4495)			
Full	2449 (83.6%)	482 (16.4%)	.481
Marginal	382 (80.9%)	90 (19.1%)	
Low	579 (83.4%)	115 (16.6%)	
Very Low	326 (81.9%)	72 (18.1%)	

1 C-reactive protein (CRP) is an inflammatory marker and has been linked to CVD and obesity (Barinas-Mitchell et al., 2001)

2 Body-mass Index (BMI) was categorized per CDC guidelines

3 Dietary inflammatory Index (DII) is based on 8 pro-inflammatory and 8 anti-inflammatory components to assess the inflammatory potential of dietary factors to provide a quantitative means for assessing the role of diet in relation to health outcomes (Kanauchi et al., 2019)

4 Food security was assessed using the US Food Security Survey Module (US FSSM). For further specifications see Methods (p. 15)

Table 2 Comparison of Included (n=4714) versus Excluded (n=2364) Participants age 12-19 NHANES 2001-06 (n=7078)

	Included n=4714	Excluded n=2364	p-value
Sex			
Male (n= 2412)	2412 (51.2%)	1129 (47.8%)	.007
Female (n=2302)	2302 (48.8%)	1235 (52.2%)	
Race/Ethnicity			
Non-Hispanic White	1329 (28.2%)	615 (26.0%)	
Non-Hispanic Black	1571 (33.3%)	794 (33.6%)	.168
Hispanic	1629 (34.6%)	847 (35.8%)	
Other	185 (3.9%)	108 (4.6%)	
CRP[1] (n=4304)			
Q1 [<.09]	2860 (60.7%)	1209 (51.1%)	
Q2 [.09-.23]	666 (14.1%)	306 (12.9%)	.000
Q3 [.23-.52]	416 (8.8%)	231 (9.8%)	
Q4 [>.52]	362 (7.7%)	207 (8.8%)	
BMI[2] (n=4620)			
Underweight [<18.5]	661 (14.3%)	269 (12.6%)	
Normal [18.5-24.9]	2514 (54.4%)	1111 (52.2%)	
Overweight [25.0-29.9]	841 (18.2%)	372 (17.5%)	.000
Obese [30.0-34.9]	349 (7.6%)	223 (10.5%)	
Morbidly Obese [>35.0]	255 (5.5%)	154 (7.2%)	
DII[3] (n=4504)			
Q1 [< -.82]	1009 (22.4%)	467 (22.6%)	
Q2 [-.82-.32]	1155 (25.6%)	526 (25.4%)	.995
Q3 [.32-1.25]	1136 (25.2%)	526 (25.4%)	
Q4 [>1.25]	1204 (26.7%)	551 (26.6%)	
Food Security[4] – Child (n=4022)			
Unaffected	2995 (74.5%)	1524 (75.9%)	
Reduced Quality or Quantity	299 (7.4%)	140 (7.0%)	
Reduced Quality and Quantity	626 (15.6%)	294 (14.6%)	
Severely Reduced Quality and Quantity	102 (2.5%)	49 (2.4%)	.670
Food Security[4] – Adult (n=4495)			
Full	2969 (66.1%)	1525 (66.7%)	
Marginal	588 (13.1%)	283 (12.4%)	.007
Low	552 (12.3%)	325 (14.2%)	
Very Low	386 (8.6%)	152 (6.7%)	
Food Security[4] – Household (n=4495)			
Full	2931 (65.2%)	1502 (65.7%)	
Marginal	472 (10.5%)	240 (10.5%)	.582
Low	694 (15.4%)	363 (15.9%)	
Very Low	398 (8.9%)	180 (7.9%)	

1 C-reactive protein (CRP) is an inflammatory marker and has been linked to CVD and obesity (Barinas-Mitchell et al., 2001)

2 Body-mass Index (BMI) was categorized per CDC guidelines

3 Dietary inflammatory Index (DII) is based on 8 pro-inflammatory and 8 anti-inflammatory components to assess the inflammatory potential of dietary factors to provide a quantitative means for assessing the role of diet in relation to health outcomes (Kanauchi et al., 2019).

4 Food security was assessed using the US Food Security Survey Module (US FSSM). For further specifications see Methods (p. 15)

Table 3 Demographics and Clinicopathological Factors of participants age 12-19 by ALT status in NHANES 2001-06 (n=4714) Split by Race/Ethnicity

		Non-Hispanic White (n=1329)			Non-Hispanic Black (n=1571)			Hispanic (n=1629)			Other (n=185)		
Variable		**Normal n=3921**	**High n=793**	**P-value**	**Normal n=3921**	**High n=793**	**P-value**	**Normal n=3921**	**High n=793**	**P-value**	**Normal n=3921**	**High n=793**	**P-value**
Sex	Male (n= 2412)	564 (84.3%)	105 (15.7%)	0.507	676 (81.3%)	155 (18.7%)	0.893	670 (82.6%)	141 (17.4%)	0.251	88 (87.1%)	13 (12.9%)	0.081
	Female (n=2302)	565 (85.6%)	95 (14.4%)		600 (81.1%)	140 (18.9%)		693 (84.7%)	125 (15.3%)		65 (77.4%)	19 (22.6%)	
CRP[1] (n=4304)	Q1 [<.09]	710 (84.9%)	126 (15.1%)	0.84	792 (80.2%)	195 (19.8%)	0.515	775 (83.8%)	150 (16.2%)	0.536	93 (83%)	19 (17%)	0.968
	Q2 [.09-.23]	156 (83.4%)	31 (16.6%)		160 (85.1%)	28 (14.9%)		216 (82.4%)	46 (17.6%)		24 (82.8%)	5 (17.2%)	
	Q3 [.23-.52]	94 (83.9%)	18 (16.1%)		110 (84%)	21 (16%)		130 (82.3%)	28 (17.7%)		12 (80%)	3 (20%)	
	Q4 [>.52]	64 (88.9%)	8 (11.1%)		104 (80%)	26 (20%)		125 (82.2%)	27 (17.8%)		6 (75%)	2 (25%)	
BMI[2] (n=4620)	Underweight [<18.5]	180 (82.9%)	37 (17.1%)	0.537	165 (81.3%)	38 (18.7%)	0.525	182 (85%)	32 (15%)	0.725	25 (92.6%)	2 (7.4%)	0.559
	Normal [18.5-24.9]	613 (84.7%)	111 (15.3%)		687 (81.1%)	160 (18.9%)		705 (83.8%)	136 (16.2%)		81 (79.4%)	21 (20.6%)	
	Overweight [25.0-29.9]	188 (87%)	28 (13%)		203 (79.3%)	53 (20.7%)		285 (84.6%)	52 (15.4%)		27 (84.4%)	5 (15.6%)	
	Obese [30.0-34.9]	88 (82.2%)	19 (17.8%)		86 (81.1%)	20 (18.9%)		97 (80.8%)	23 (19.2%)		14 (87.5%)	2 (12.5%)	
	Morbidly Obese [>35.0]	39 (90.7%)	4 (9.3%)		106 (86.9%)	16 (13.1%)		68 (80%)	17 (20%)		4 (80%)	1 (20%)	

		Non-Hispanic White (n=1329)			Non-Hispanic Black (n=1571)			Hispanic (n=1629)			Other (n=185)		
Variable		**Normal n=3921**	**High n=793**	**P-value**	**Normal n=3921**	**High n=793**	**P-value**	**Normal n=3921**	**High n=793**	**P-value**	**Normal n=3921**	**High n=793**	**P-value**
DII[3] (n=4504)	Q1 [< -.82]	270 (85.2%)	47 (14.8%)	0.98	254 (81.7%)	57 (18.3%)	0.573	298 (87.1%)	44 (12.9%)	0.027	32 (82.1%)	7 (17.9%)	0.99
	Q2 [-.82-.32]	263 (84.8%)	47 (15.2%)		278 (79.4%)	72 (20.6%)		380 (84.3%)	71 (15.7%)		37 (84.1%)	7 (15.9%)	
	Q3 [.32-1.25]	275 (85.4%)	47 (14.6%)		319 (83.3%)	64 (16.7%)		305 (79.2%)	80 (20.8%)		38 (82.6%)	8 (17.4%)	
	Q4 [>1.25]	284 (84.3%)	53 (15.7%)		368 (80.5%)	89 (19.5%)		305 (85%)	54 (15%)		43 (84.3%)	8 (15.7%)	
Food Security[4] – Child (n=4022)	Unaffected	821 (84.1%)	155 (15.9%)	0.576	741 (80.8%)	176 (19.2%)	0.861	820 (83.9%)	157 (16.1%)	0.838	102 (81.6%)	23 (18.4%)	0.309
	Reduced Quality or Quantity	36 (92.3%)	3 (7.7%)		107 (81.7%)	24 (18.3%)		98 (85.2%)	17 (14.8%)		14 (100%)	0 (0%)	
	Reduced Quality and Quantity	62 (84.9%)	11 (15.1%)		187 (78.9%)	50 (21.1%)		256 (84.8%)	46 (15.2%)		12 (85.7%)	2 (14.3%)	
	Severely Reduced Quality and Quantity	9 (81.8%)	2 (18.2%)		39 (78%)	11 (22%)		31 (79.5%)	8 (20.5%)		2 (100%)	0 (0%)	
Food Security[4] – Adult (n=4495)	Full	887 (84.5%)	163 (15.5%)	0.61	735 (81.4%)	168 (18.6%)	0.732	741 (84.9%)	132 (15.1%)	0.408	116 (81.1%)	27 (18.9%)	0.651
	Marginal	70 (88.6%)	9 (11.4%)		184 (79.7%)	47 (20.3%)		216 (81.2%)	50 (18.8%)		11 (91.7%)	1 (8.3%)	
	Low	54 (84.4%)	10 (15.6%)		148 (82.2%)	32 (17.8%)		249 (84.1%)	47 (15.9%)		11 (91.7%)	1 (8.3%)	
	Very Low	63 (88.7%)	8 (11.3%)		134 (78.4%)	37 (21.6%)		106 (80.9%)	25 (19.1%)		11 (84.6%)	2 (15.4%)	

		Non-Hispanic White (n=1329)			Non-Hispanic Black (n=1571)			Hispanic (n=1629)			Other (n=185)		
Variable		**Normal n=3921**	**High n=793**	**P-value**	**Normal n=3921**	**High n=793**	**P-value**	**Normal n=3921**	**High n=793**	**P-value**	**Normal n=3921**	**High n=793**	**P-value**
Food Security[4] – Household (n=4495)	Full	884 (84.4%)	163 (15.6%)	0.672	719 (81.6%)	162 (18.4%)	0.834	733 (84.9%)	130 (15.1%)	0.217	113 (80.7%)	27 (19.3%)	0.487
	Marginal	61 (88.4%)	8 (11.6%)		145 (79.2%)	38 (20.8%)		165 (79.3%)	43 (20.7%)		11 (91.7%)	1 (8.3%)	
	Low	69 (86.3%)	11 (13.8%)		197 (80.4%)	48 (19.6%)		298 (84.4%)	55 (15.6%)		15 (93.8%)	1 (6.3%)	
	Very Low	60 (88.2%)	8 (11.8%)		140 (79.5%)	36 (20.5%)		116 (81.7%)	26 (18.3%)		10 (83.3%)	2 (16.7%)	

1 C-reactive protein (CRP) is an inflammatory marker and has been linked to CVD and obesity (Barinas-Mitchell et al., 2001)

2 Body-mass Index (BMI) was categorized per CDC guidelines

3 Dietary inflammatory Index (DII) is based on 8 pro-inflammatory and 8 anti-inflammatory components to assess the inflammatory potential of dietary factors to provide a quantitative means for assessing the role of diet in relation to health outcomes (Kanauchi et al., 2019).

4 Food security was assessed using the US Food Security Survey Module (US FSSM). For further specifications see Methods (p. 15)

Table 4 Predictors of ALT Status in Participants age 12-19 in NHANES 2001-06 (n=4714)

	Univariate Model OR (95% CI)	Multivariate Model OR (95% CI)
Sex		
Male (ref)	1.00	1.00
Female	.951 (.816-1.11)	.98 (.82-1.17)
Race/Ethnicity		
NHW (ref)	1.00	1.00
NHB	1.31 (1.07-1.59)	1.25 (1.00-1.57)
Hispanic	1.10 (0.92-1.35)	.99 (.79-1.25)
Other	1.18 (0.78-1.78)	.98 (.61-1.58)
CRP[1] (n=4304)		
Q1 [<.09]	1.00	1.00
Q2 [.09-.23]	.96 (.76-1.20)	.94 (.72-1.22)
Q3 [.23-.52]	.98 (.74-1.23)	.87 (.63-1.22)
Q4 [>.52]	1.02 (.76-1.36)	1.13 (.80-1.59)
BMI[2] (n=4620)		
Underweight [<18.5]	1.00	1.00
Normal [18.5-24.9]	1.04 (.83-1.31)	1.04 (.81-1.33)
Overweight [25.0-29.9]	.99 (.76-1.31)	1.11 (.82-1.50)
Obese [30.0-34.9]	1.14 (.81-1.60)	1.12 (.75-1.66)
Morbidly Obese [>35.0]	.89 (.59-1.33)	1.04 (.66-1.63)
DII[3] (n=4504)		
Q1 [< -.82]	1.00	1.00
Q2 [-.82-.32]	1.13 (.90-1.43)	1.23 (.95-1.59)
Q3 [.32-1.25]	1.17(.93-1.47)	1.31 (1.01-1.69)
Q4 [>1.25]	1.12 (.89-1.41)	1.14 (.88-1.48)
Food Security[4] – Child (n=4022)		
Unaffected	1.00	1.00
Reduced Quality or Quantity	.84 (.60-1.17)	.63 (.37-1.09)
Reduced Quality and Quantity	1.03 (.82-1.29)	.89 (.51-1.54)
Severely Reduced Quality and Quantity	1.26 (.77-2.06)	1.04 (.47-2.29)
Food Security[4] – Adult (n=4495)		
Full	1.00	1.00
Marginal	1.13 (.89-1.42)	.58 (.22-1.51)
Low	.99 (.77-1.26)	.54 (.17-1.68)
Very Low	1.16 (.88-1.53)	1.11 (.27-4.55)
Food Security[4] – Household (n=4495)		
Full	1.00	1.00
Marginal	1.19 (.93-1.54)	2.08 (.80-5.41)
Low	1.01 (.81-1.26)	2.03 (.53-7.75)
Very Low	1.12 (.85-1.48)	1.26 (.23-6.75)

1 C-reactive protein (CRP) is an inflammatory marker and has been linked to CVD and obesity (Barinas-Mitchell et al., 2001)

2 Body-mass Index (BMI) was categorized per CDC guidelines

3 Dietary inflammatory Index (DII) is based on 8 pro-inflammatory and 8 anti-inflammatory components to assess the inflammatory potential of dietary factors to provide a quantitative means for assessing the role of diet in relation to health outcomes (Kanauchi et al., 2019).

4 Food security was assessed using the US Food Security Survey Module (US FSSM). For further specifications see Methods (p. 15)

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